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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SOLOLA, TAOFIQ A	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,687	AVIV ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 8/19/03 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-24 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of claims 21-24 is for "preventing" or "alleviating" neurological disorders, chronic degenerative diseases, CNS poisoning, cognitive impairment, etc., with compound of formula I.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to prophylactic effects on the above listed diseases, whether or not the disease is effected by the blocking of NMDA receptor would make a difference.

Applicants are claiming a method of "preventing" or "alleviating" neurological disorders, chronic degenerative diseases, CNS poisoning, cognitive impairment, etc., by administering compound of formula I.

The obstacles to prevention of neurological diseases in humans are well documented in the literature. See, for example, KN Prassad, J. Postgrad. Med. 49 (2003 pages 236-245.

According to Prassad, no preventive or long-term effective strategies are available for neurological disorders. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting the prevention or alleviation of the listed neurological diseases on its face. Additionally, there is no evidence in the specification that established correlation between applicant experiment and prevention or alleviation of the listed neurological disorders. See Ex parte Mass, 9 USPQ2d 1746, 1987. Therefore, the quantity of experimentation required to use the compound as claimed, based on applicant's limited disclosure would be undue burden because, one of ordinary skill in the art would have to perform significant amount of experiments

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification are the investigations in rats, rabbits and monkeys as well as clinical trials (phase I and II) in humans. There are no working examples present for the prevention or alleviation of the listed neurological disorders.

The breadth of the claims

The breadth of the claims is for prevention or alleviation of the listed neurological disorders.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which neurological disorder out of all relevant disorders would be benefited (preventable) by the blockage of NMDA receptor. Such is deemed an undue experimentation.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which neurological disorder is preventable or could be alleviated.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the prevention or alleviation of the listed neurological disorders. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by the compound of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which neurological diseases are preventable or alleviated by the compound of the instant claims, with no assurance of success.

This rejection can be overcome deleting "preventing", "alleviating" and "prophylactically" from claim 21.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 7-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims improperly depend from claim 4. Claim 4 is drawn to a composition and therefore, inherently comprises a pharmaceutical carrier or diluent. Hence, claim 7 is a substantial duplicate of claim 4. By adding claim 7 to 4 the rejection would be overcome.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 15-16, 18-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Kloog et al., US 5,284,867.

Kloog et al., disclose the instantly claimed compound (HU-211), essentially free of the (3R,4R) enantiomer, various pharmaceutical formulations (compositions) for various types of administrations (columns 4-5) and methods of use for treating neurological disorders. The formulation is emulphor or emulsions and may contain antioxidants, preferably the antioxidant is α-tocopherol. See example 3, column 12 and column 13, lines 1-5. Kloog et al., also disclose various % combinations of the emulsions in column 13, lines 5 to 23.

Applicant should note that the phraseology "essentially free of the (3R,4R) enantiomer" is deemed (3S,4S) enantiomer is in enantiomeric excess of at least 99.90 % over the (3R,4R) enantiomer absent a showing to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kloog et al., US 5,284,867.

Applicant claims the (3S,4S) enantiomer of compound I having enantiomeric excess of at least 99.90 % over the (3R,4R) enantiomer, the composition and method of use for treating various neurological disorders. The composition comprise co solvents such as polyoxyl 35 castor oil from 30-80 % W/W, ethanol from 20-70 % W/W and 0.001-0.1 % w/w of edetic acid. Applicant also claims composition having 0.1-5 % W/W of α-tocopherol.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kloog et al., teach the instantly claimed compound (HU-211), essentially free of the (3R,4R) enantiomer, various pharmaceutical formulations (compositions) for various types of administrations (columns 4-5) and methods of use for treating neurological disorders. The composition comprise co solvents such as ethanol, glycerol, PEG and PPG. Kloog et al., also teach composition having 0.02 % W/W of α-tocopherol. See columns 12-13.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant invention and that of Kloog et al., is that applicant claims the instant compound having (3S,4S) enantiomeric excess of at least 99.90 % over the (3R,4R) enantiomer, while Kloog et al., teach the compound as essentially free of the (3R,4R) enantiomer. Also, applicant is claiming co solvents such as polyoxyl 35 castor oil from 30-80 % W/W, ethanol from 20-70 % W/W and 0.001-0.1 % W/W of edetic acid, while Kloog et al., do not teach polyoxyl 35 castor oil, edetic acid or % W/W of ethanol.

Finding of prima facie obviousness---rational and motivation (MPEP §2142.2413)

However, there is no evidence that the compound of Kloog et al., does not have (3S,4S) enantiomeric excess of at least 99.90 % over the (3R,4R) enantiomer. Even if the instantly claimed compound is substantially purer than the compound of Kloog et al., and there are new and novel properties, functions or utilities arising from the higher level of purity, such would not make the instant invention patentable over the prior art of Kloog et al. Something old does not become new upon discovery of new properties (e.g. purification level), functions or utilities. *In re Best*, 562 F.2d 1252; 195 USPQ 430 (CCPA, 1977). Also, the addition of an inert carrier, such as co solvents, to a non-patentable compound is not patentable. *Ibid.* Claiming 20-70 % ethanol and 0.1-5 % α-tocopherol are obvious modifications available to the special preference of an artisan. They are mere optimization of variables, which are not patentable absent unexpected result due to each variable, which is different in kind and not merely in degree from that of the prior art. *In re Aller,* 22 F.2d 454,105 USPG 233 (CCPA, 1955).

Therefore, the instant invention is prima facie obvious from the teaching of Kloog et al. One of ordinary skill in the art would have known to claim compound of formula I as (3S,4S) enantiomeric excess of at least 99.90 % over the (3R,4R) enantiomer at the time this invention was made. The motivation is from the teaching of Kloog et al., that the compound is essentially free of the (3R,4R) enantiomer.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD, JD, whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

TAOFIQ SOLOLA
PRIMARY EXAMINER

Group 1626

September 29, 2004